



A Systemic Review on Covid 19

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KEYWORDS

prescription pattern, treatment pattern, both waves, complication, sign, and symptoms.

ABSTRACT:

Introduction: The coronavirus is a respiratory ailment that is characterised by its acute nature and is produced by a specific strain of coronavirus in the human population. This particular virus has the potential to induce severe symptoms and, in certain instances, lead to mortality particularly among elderly individuals and those with pre-existing health disorders.. The emergence of the virus was first observed in China in 2019, and subsequently escalated into a global pandemic in 2020.

The Corona Virus is classified as a positive-sense, single-stranded, non-segmented Ribonucleic acid virus. It is a member of the Coronaviridae family within the Nidovirales order. This family has a wide range of viruses that can cause sickness in both animals and humans. The study includes different variants of covid-19 and various symptoms, they used different diagnostic methods to identify the covid-19, supportive care, vaccines, and medicines are under investigation.

Aim: The main aim of this study was to investigate and provide insights into the pertinent clinical concerns and overview the health complication commonly observed in individuals who have diagnosed with covid-19.

Methodology: Study design: Systematic review

Study site: online databases like PubMed, Lancet, BMJ

Study duration: November 2021-May 2022

Study sample: 30 articles were collected with key ideas

Study criteria:

Inclusion:

- Studies performed on human subjects
- Articles published in 2020-2022
- Manuscript titles like-covid-19, prescription patterns, treatment pattern, symptoms, systemic review, complications, first wave and second wave
- Articles of Age group above 18 years
- Articles published in countries like –India, USA, Spain, Nigeria, Italy, UK, California.

Exclusion:

- Articles of age group below 18 years are excluded
- Articles with pregnant women subjects are excluded
- Articles published in countries like – Australia, Africa, and Europe.
- Articles of animal studies are excluded.

Results and Discussion: In this study, we reviewed different articles on symptoms, risk factors, co-morbidities, treatment patterns, and both 1st and 2nd waves of covid-19.

Conclusion: Younger adults are disproportionately affected during the second phase, while older adults with co-morbidities are more significantly impacted during the first. While symptomatic treatment is administered during both waves, the second wave necessitates the use of corticosteroids and oxygen therapy primarily due to respiratory complications.



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List of ABBREVIATIONS

SARS – Severe Acute Respiratory System
 Co-V – Corona Virus
 RNA – Ribo Nucleic Acid
 MERS – Middle East Respiratory Syndrome
 WHO – World Health Organization
 ICTV – International Committee on Taxonomy of Viruses
 COVID-19 – Corona Virus Disease in 2019
 GISAID – Global Initiative on Sharing All Influenza Data
 UK – United Kingdom
 VOC – Vaso Occlusive Disease
 RT-PCR – Reverse Transcription-Polymerase Chain Reaction
 BD – Bis per Day
 GP – General Practitioner
 COLCH – Colchicine
 ROSU – Rosuvastatin
 FTC – Emtricitabine
 TDF – Tenofovir
 ICU – Intensive Care Unit
 CHF – Congestive Heart Failure
 COPD – Chronic Obstructive Pulmonary Disease
 DVT – Deep Vein Thrombosis
 GERD – Gastro-Esophageal Reflux Disease
 AIDS – Acquired Immune Deficiency Syndrome
 HIV – Human Immune deficiency Virus



SABA – Supplied Air Breathing Apparatus
 ICS – Inhaled Corticosteroids
 ARB – Angiotensin Receptor Blockers
 ACE – Angiotensin Converting Enzyme
 NSAID – Non-Steroidal Anti-Inflammatory Drug
 PPI – Proton Pump Inhibitors
 H2RA – Histamine 2 Receptor Antagonist
 ATC – Anatomical and Therapeutic Classification

APPENDICES

Appendices	IEC approval letter at BCP
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Covid-19: Definition

The coronavirus is a respiratory ailment of acute nature that is produced by a specific strain of the corona virus in the human population. This virus has the potential to induce severe symptoms and, in certain instances, result in mortality, particularly among the elderly and individuals with pre-existing health issues. The novel coronavirus, known as COVID-19, was first detected in

the country of China in 2019 and then escalated to a global pandemic in the year 2020. Corona virus Disease is an infectious disease induced by the SARS-COV-2-Virus.

Corona Virus is a positive-sense single-stranded non-segmented Ribose Nucleic Acid virus that belongs to the Coronaviridae family's Nidovirales order. (a big viral family that causes sickness in animals or people).

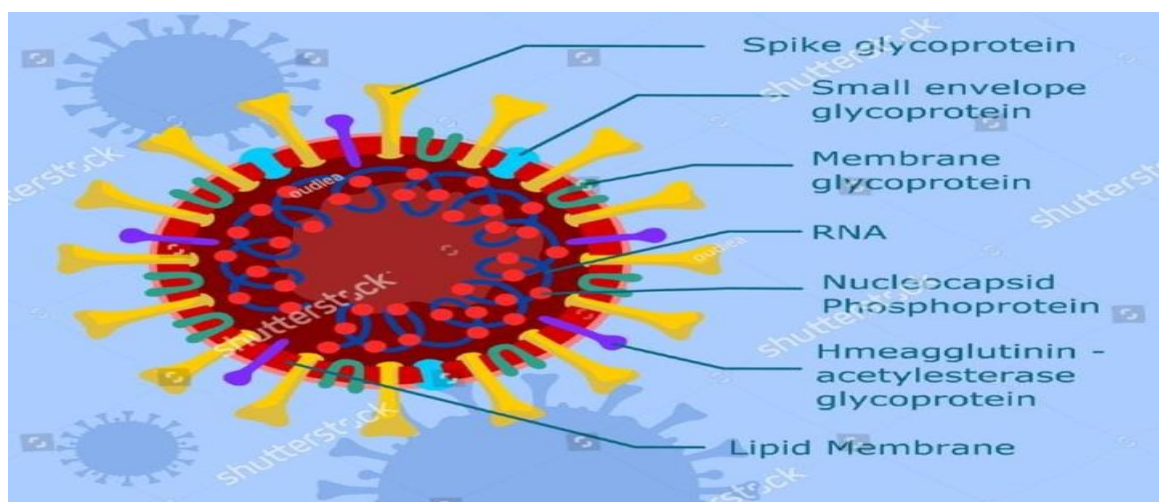


Fig 1.1: coronavirus structure. ⁽⁴³⁾

Co-Vs is a Zoonotic disease.

Respiratory infections induced by these viral pathogens encompass a spectrum of manifestations, spanning from mild ailments such as the common cold to more serious conditions like MERS and SARS. Notably, these infections can lead to fatalities, particularly among elderly individuals and those with pre-existing health conditions..

The declaration of the coronavirus disease 2019 as a pandemic has been made by the World Health Organisation (WHO). In certain nations, a collaborative endeavour was required to mitigate the further transmission of the virus..

A pandemic is characterised as an event that transpires throughout a vast geographical expanse and impacts a notably significant fraction of the populace. ^(1,41)

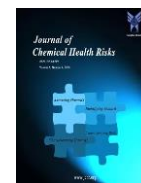
COVID-19 is a strain of Corona Viruses. Its name was announced on 11 Feb 2020.

SARS-Co-V 2

SARS-CoV-2 is a novel variant that has not been previously detected in the human population.

The announcement of the name was made by the International Committee on Taxonomy of Viruses (ICTV) on February 11, 2020.

Genetically, this virus exhibits a close relationship to the Corona virus, which was associated with the severe acute respiratory syndrome (SARS) epidemic that occurred in 2003. However, it should be noted that the two viruses exhibit distinct characteristics and behaviours.



In the year 2019, a novel strain of coronavirus, known as COVID-19, was first found in the city of Wuhan, located in the People's Republic of China. The coronavirus is classified as a diverse group of viruses that can induce a range of illnesses, spanning from mild symptoms resembling the common cold to more severe conditions such as Middle East Respiratory Syndrome (MERS) and severe acute respiratory syndrome (SARS). The coronavirus is a prevalent viral pathogen that can lead to infections in the sinuses, nasal passages, and upper respiratory tract.⁽⁵⁾

The novel coronavirus, or COVID-19, poses a significant threat due to the absence of a specific treatment and its rapid progression leading to multi-organ failure. These viral groups are responsible for inducing detrimental diseases in avian species as well as mammalian species.

- In the human population, the virus is known to induce moderate respiratory illnesses, although in rare instances, it may lead to fatal outcomes.⁽⁴³⁾
- The ingestion of this substance in animals such as cows and pigs has been seen to result in the manifestation of diarrhoea.
- In chickens it causes severe respiratory infection.

The coronavirus is classified within the subfamily Orthocoronavirinae. The nucleocapsid, which encompasses the single-stranded RNA genome, exhibits a helical structure and is enclosed within an envelope-like frame. Its size typically falls within the range of 26-

32 kilobases, providing a distinct and precise characterization. COVID-19 represents the most extensive classification of RNA viruses. Identifying whether the fever is caused by the coronavirus or another virus that causes the common cold is sometimes challenging in the majority of instances. Now newly detected a common cause for corona virus is pneumonia and other respiratory infections. Healthcare professionals are actively engaged in combatting this condition and directing their attention towards identifying factors that contribute to improved results. In December 2019, a group of pneumonia patients was observed in Wuhan, China.⁽⁷⁾ Several of the newly reported cases were individuals who had visited or worked in seafood and live animal marketplaces located in Wuhan. The aetiology of the disease was determined through an investigative inquiry, which revealed that the newly identified coronavirus was the causative agent. Consequently, the illness was officially designated as COVID-19. The transmission of the Covid-19 virus originated in China and then extended to many regions across the globe. On January 30, 2020, the World Health Organisation declared the outbreak as a Public Health Emergency of International Concern. The coronavirus is a diverse family of viruses characterised by the presence of a genetic material enclosed within a lipid envelope, which exhibits protein spikes that resemble a crown-like structure. The term "corona" is an alternative designation for the crown, which is why this virus is referred to by this name.

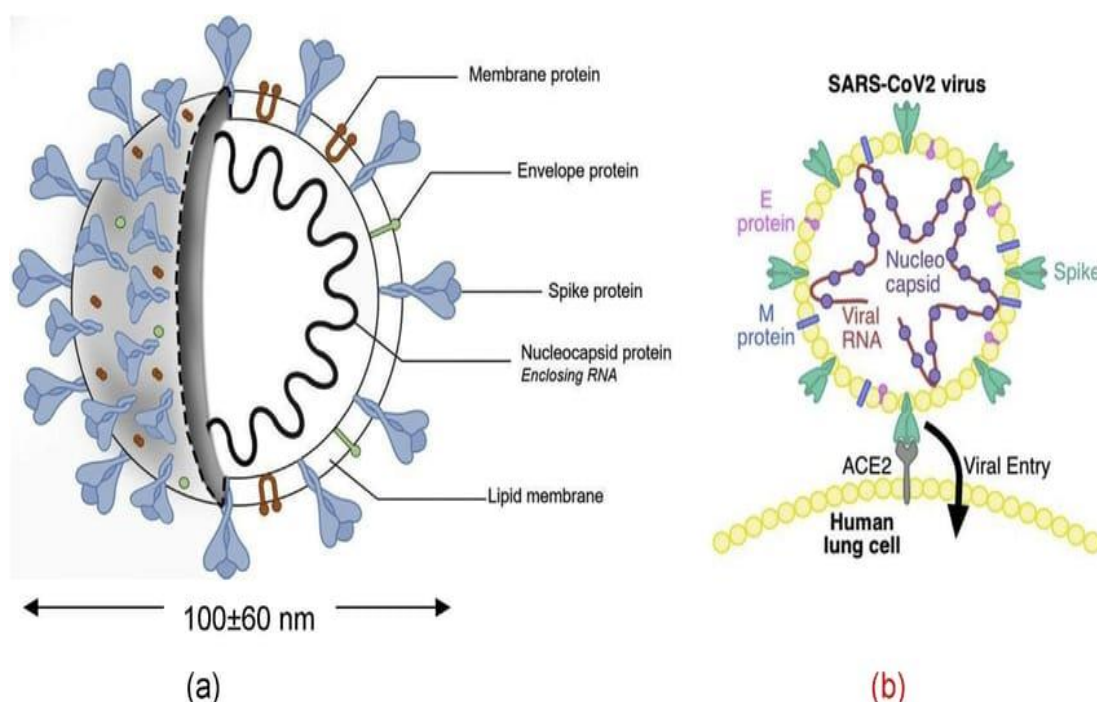


Fig 1.2: coronavirus complete picture.⁽⁴⁷⁾



There exist various classifications of coronaviruses that induce disease in both animal and human populations. Coronaviruses have the potential to induce a spectrum of respiratory conditions in people, ranging from mild common cold symptoms to more severe infections. The viruses mentioned encompass severe acute respiratory syndrome – corona virus (SARS-CoV), which was initially detected in China in 2003, Middle East respiratory syndrome – corona virus (MERS-CoV), first identified in Saudi Arabia in 2012, and SARS-CoV-2, initially documented in Wuhan, China in 2019.⁽²⁾

Origin of the virus:

The coronavirus exhibits a broad host range, with the potential for zoonotic transmission to humans, a phenomenon commonly referred to as spillover^(1,4)

The potential causes of this phenomenon encompass a variety of elements, including viral alterations and heightened interactions between people and animals. For instance, Middle East Respiratory Syndrome Coronavirus (MERS-CoV) is transmitted through camels, while Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) is transmitted from felines exhibiting severe symptoms.⁽¹²⁾

Transmission:

This disease has the potential to be transmitted via person-to-person contact through respiratory droplets. When an individual who is afflicted expels respiratory droplets by actions such as coughing, walking, and sneezing. Transmission can also occur through close contact between an individual and an infected person. When an infected individual comes into contact with materials, there is a risk of transmission if another person subsequently touches those objects and then touches their eyes, nose, or mouth.⁽⁴⁾

Variants

The SARS-CoV-2 virus exhibits a multitude of variants, numbering in the thousands, which can be categorised into distinct groups known as categories or families. The World Health Organisation (WHO), in collaboration with many partners, expert networks, national authorities, institutions, and academics, has developed nomenclature systems to monitor and designate genetic lineages of SARS-CoV-2. These systems include GISAID, Nextstrain, and Pango. Currently, the World Health Organisation (WHO) has advised the utilisation

of Greek alphabet letters, such as Alpha, Beta, Delta, and Gamma, for the purpose of designating variants. The subsequent lineage categorises the Variants into five distinct clades, namely 19A, 19B, 20A, 20B, and 20C. GISAID classifies these into seven distinct lineages, namely L, O, V, S, G, GH, and GR. As of December 2021, there exist five prevailing forms of SARS-CoV-2 that are disseminating within communities.

1) The Alpha variety (B.1.1.7), commonly referred to as the UK variety, was initially detected in London and Kent.

2) The Beta Variant, also known as B.1.351 or the South Africa Variant,

3) The Gamma Variant, often known as P.1 or the Brazil Variant,

4) The Delta Variant, also known as B.1.617.2 or the India Variant,

5) The Omicron Variant (B.1.1.529), as of December 7th, had been detected in 57 countries.⁽²⁾

Alpha: The mutation observed in the alpha version affects the spike protein, a crucial component facilitating the viral infection of its host. Several studies have established a potential association between this particular variation and an increased likelihood of mortality. However, it is important to note that the supporting evidence is not robust or conclusive.⁽¹⁹⁾

Beta: The beta variation demonstrates a higher transmissibility rate compared to the original virus, although does not exhibit a heightened severity of sickness.

Gamma: The gamma variant has a higher level of transmissibility compared to preceding strains of the virus.

Delta: The alterations in the spike protein of the delta variant have been observed to potentially enhance its transmissibility by up to 50% compared to other individuals infected with the COVID-19 virus.

Omicron:

The omicron form has a substantial quantity of mutations, including but not limited to T951 and T478, among others, some of which have raised notable concerns. Preliminary findings indicate a heightened susceptibility to re-infection associated with this variant in comparison to other variants of concern (VOCs). Several ongoing investigations are being conducted to assess the characteristics and implications of this particular variant.⁽³⁾

Variant	WHO designation	Classification	Country/Region of Origination
B.1.1.7	Alpha	Variant of concern	United Kingdom
B.1.351	Beta	Variant of concern	South Africa
P.1	Gamma	Variant of concern	Brazil
B.1.617.2	Delta	Variant of concern	India
B.1.1.529	Omicron	Variant of concern	South Africa

Table 1.1: Different variants of covid-19. ⁽¹²⁾



Causes:

Researchers have empirically determined that certain factors are causative agents of the disease.

a) The consumption of marine organisms, such as sealife, and terrestrial animals, such as bats, pigs, snakes, etc.

b) Animal pathogens: Each animal possesses a distinct physiology and harbours microorganisms within their body. Consuming these animals can potentially lead to incompatibilities within the human system, hence increasing the likelihood of illness manifestation.

Transmission: The transmission of the coronavirus can occur through direct contact with contaminated surfaces or objects that have been touched by an infected individual and then come into contact with an unaffected individual.

Individuals without specialised training or knowledge may inadvertently come into contact with their nose, eyes, or mouth, so facilitating the transmission of infections. ⁽⁹⁾

Symptoms:

Most people with COVID-19 can occur mild to moderate symptoms and recover without special treatment. However, some will become seriously ill and require medical attention.

a) Most Common Symptoms

- Fever
- Cough
- Tiredness
- Loss of taste or smell

b) Less Common Symptoms

- Sore throat
- Headache
- Aches and pains
- Diarrhea
- A rash on the skin, or discoloration toes or fingers
- Red or irritated eyes

C) Serious Symptoms

- Difficulty Breathing or Shortness of breath
- Loss of speech or mobility, or confusion.
- Chest pain. ^(28,30)

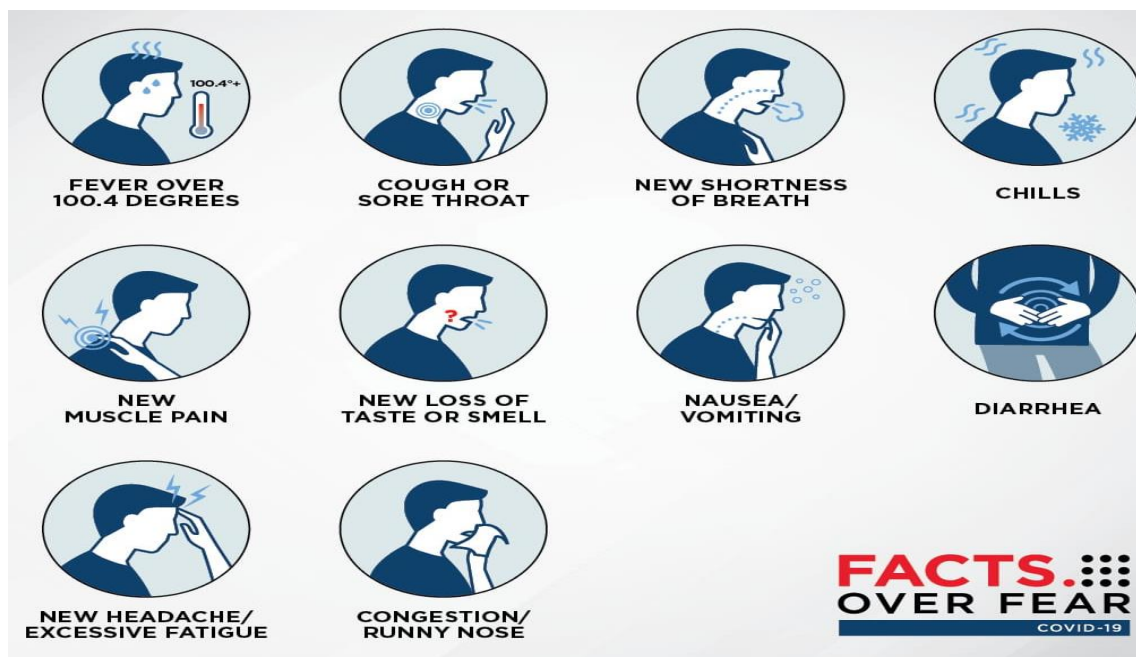


Fig 1.3: coronavirus symptoms⁽⁴⁶⁾

It is imperative to promptly seek medical assistance if one is experiencing severe symptoms. Individuals without specialised training or knowledge may inadvertently come into contact with their nose, eyes, or mouth, so facilitating the transmission of infections.

Individuals with minor symptoms should be capable of effectively managing their symptoms within the confines of their own residence. The manifestation of symptoms often occurs during a period of around 5 to 6 days following the transmission of a viral infection to an individual. After exposure to the Virus, Symptoms may begin in 1-14 days.

The majority of individuals, approximately 81%, experience mild to moderate symptoms, such as mild pneumonia. A smaller proportion, around 14%, develop severe symptoms characterised by dyspnea, hypoxia, or more than 50% lung involvement as observed through imaging. A further 5% of individuals experience critical symptoms, including respiratory failure, shock, or

individual. After exposure to the Virus, Symptoms may begin in 1-14 days.



multiorgan dysfunction. Older individuals are at a heightened risk of experiencing severe symptoms.

Pathogenesis:

- The virus is a single-stranded RNA virus with protein spikes, enters the host's respiratory system through the air..
- It enters and attached to the S1 subunit of viral spike protein allows the virus to bind to the host cell receptor ACE-2.
- They start reproducing themselves by undergoing cellular mechanism
 - a) By the viral spike protein conformational changes takes place. It penetrates into S2 Subunit of Spike protein
 - b) By S2 subunit of spike protein/receptor mediated endocytosis, viral and host cell membrane Fusion takes place.
 - c) Release of viral contents by the entry of viral nucleocapsid into host cell
 - d) The contents of the virus undergo
 - 1} Viral RNA replication
 - 2} Transcription and
 - 3} Translation

- By Maturation new viral particles are released by protein biosynthesis in the cytoplasm.
- Newly formed particles from the virus are transported to the cell membrane via Golgi, Vesicles and Exocytosis to the extra cellular space and forms a large quantity of new cells.
- If the infection is mild, people does not develop any symptoms, but when they sneeze, cough or cold, they can act as a carrier.
- Depending upon severity of infection and other factors, symptoms may appear between 2-14 days known as Incubation period.
- Severe Lung damage can cause buildup of fluid within and around the lungs called ARDS (acute respiratory distress syndrome).
- In severe cases, patient Blood pressure falls drastically develop septic shock.
- Body starves for oxygen and without oxygen, organ begins falls because of septic shock.
- Main causes of death are ARDS and Septic Shock.
- Factors like >60 years, Smoking, Previous medical condition like Hypertension increases the severity of death.

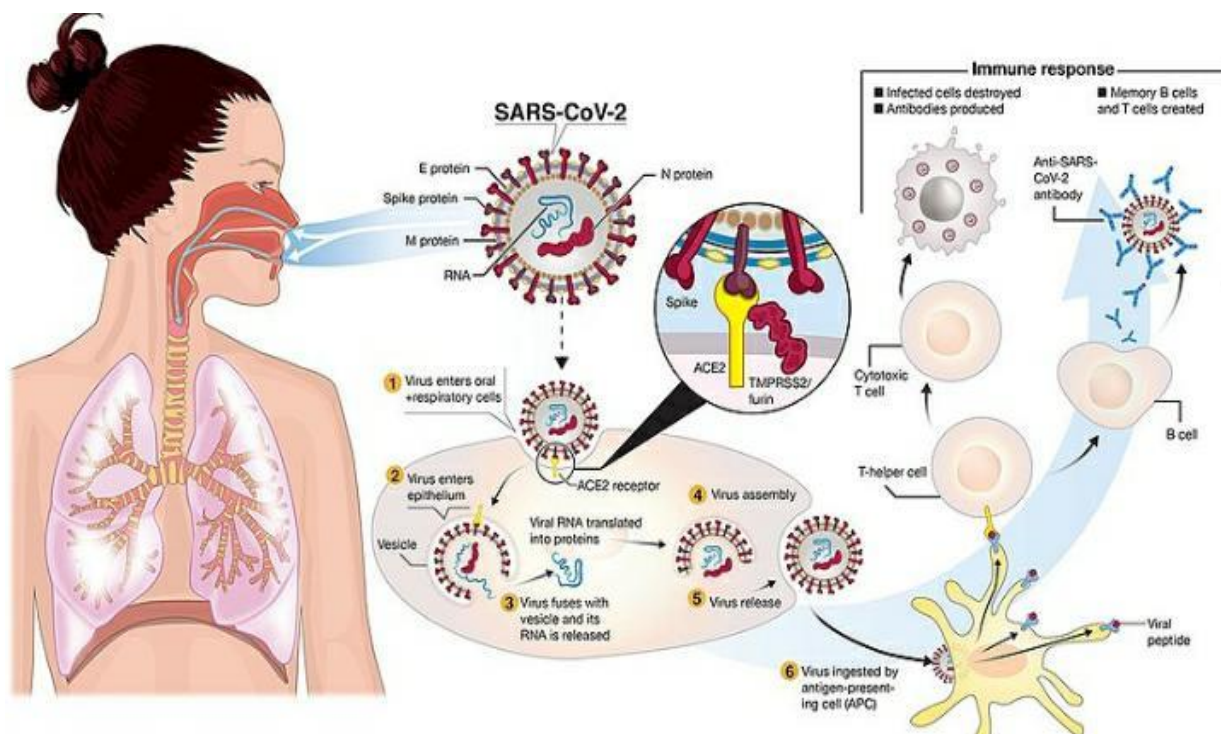
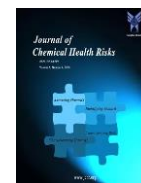


Fig 1.4: coronavirus pathogenesis. ⁽²⁹⁾

Pathophysiology:

- The SARS-CoV-2 virus has the ability to infect a diverse array of cells inside the human body, leading to a variety of associated symptoms.

- The coronavirus typically impacts the upper respiratory system, leading to infections in the sinuses, nose, and throat, as well as the lower respiratory tract, resulting in infections in the windpipe and lungs.



- Covid-19 has a direct impact on the respiratory system, particularly the lungs, which are the primary organs affected by this viral infection. The virus primarily targets and causes damage to the alveoli, which are small air sacs within the lungs.
- The SARS-CoV-2 virus utilises the angiotensin-converting enzyme 2 (ACE2) receptor, primarily found on the surface of type-II alveolar cells in the lungs, as its point of entry into host cells.
- Specifically, the virus binds to a surface glycoprotein known as the "spike protein" in order to establish a connection with the ACE2 receptor and facilitate its entry into the host cell. ^(8,30)

Complications:

- Pneumonia
- Viral sepsis
- Acute Respiratory Distress Syndrome
- Kidney failure
- Cytokine release syndrome
- Respiratory failure
- Pulmonary fibrosis
- Pediatric Multisystem Inflammatory Syndrome
- Long Covid. ^(10,17)

Diagnosis:

The US-FDA approves the diagnostic testing for diagnosis of COVID-19 are:

1) RT-PCR test (Molecular test)

By using reverse transcription polymerase chain reaction (RT-PCR), this test detects the genetic material of virus.

In this test, the health care professional inserts a long nasal swab called Nasopharyngeal swab into the nostril and collects fluid sample from the back of nose.

The fluid sample in the nostrils may be collected by using mid-turbinate swab (a shorter nasal swab) or anterior nares swab (or very short swab). In some cases, the health care professional inserts a long swab called oropharyngeal swab into the back of throat. Or RT-PCR test are very accurate.⁽¹⁶⁾

2) Antigen test

This assay is capable of identifying specific viral proteins. A fluid sample can be obtained through the utilization of a lengthy nasal swab.

Treatment:

The treatment for corona virus is not at identified, but by following prevention measures decrease the symptoms of this disease. it includes:

a) Self-care: Currently, there is no specific vaccine available for the treatment of the coronavirus. Therefore, it is imperative that we adopt preventive

measures to mitigate the risk of contracting the disease. These measures include practising regular hand hygiene by thoroughly washing hands with soap and warm water, wearing masks when venturing outside, maintaining the use of hand sanitizers, and refraining from touching the eyes, nose, and mouth with unwashed hands. It is advisable to refrain from engaging in close contact with individuals who have been afflicted. ⁽¹⁶⁾

Those who exhibit no symptoms or experience minor symptoms

- It is recommended to seclude oneself within a sufficiently ventilated enclosure.
- It is recommended to utilise a medical mask with three layers. The mask should be disposed of after a duration of 8 hours or sooner if it becomes damp or visibly soiled.
- In the event that a carer needs to enter the isolated room of a patient, it is advisable for both the carer and the patient to consider utilising a N95 mask.
- The mask should only be destroyed once it has been disinfected using a solution of 1% sodium hypochlorite.
- It is advisable to engage in periods of rest and relaxation.
- In order to sustain proper hydration, it is recommended to consume a substantial amount of fluids.
- Frequent hand washing with soap and water for a minimum duration of 40 seconds, or regular use of alcohol-based sanitizers for hand hygiene, is recommended.
- It is advised not to share personal belongings with others. ⁽²⁵⁾
- The recommended practice is to sanitize frequently touched surfaces in the room, such as doorknobs and handles, using a 1% hypochlorite solution.
- The temperature and pulse rate are monitored on a daily basis.
- The practice of regularly monitoring oxygen saturation levels using pulse oximetry on a daily basis. ⁽²¹⁾
- In the event of any exacerbation of symptoms, it is advisable to promptly seek consultation with a medical professional. ⁽³⁶⁾

b) Instruction for care givers:

- Mask: The carer is advised to utilize a medical mask with three layers. The utilization of N95 masks could be contemplated. When the carer is present in the same room as the one who is unwell.
- Hand hygiene: Hand hygiene is a crucial practice for carers, particularly when they have had contact with an unwell individual or the near environment of a patient.
- Risk of exposure: In order to minimize the risk of exposure to patient-related body fluids such as oral or



respiratory secretions, it is advisable to refrain from direct contact with the patient or their immediate environment.

While handling the patient, always use the disposable gloves. Hand Hygiene is done before and after disposing the gloves. ⁽³⁴⁾

c) Food management:

Taking a protein rich food, nuts and drinking more fluids may also decreases the symptoms caused by the disease.

d) Management with Drugs:

Currently, there are no specific pharmaceutical interventions available. However, certain over-the-counter medications have been found to alleviate symptoms such as cold, sore throat, and body aches. However, over-the-counter medications are not recommended for administration to anyone under the age of 19. Certain medications such as Ibuprofen and Acetaminophen provide symptomatic relief but do not offer a definitive solution for the underlying condition. Clinical management include the timely deployment of infection prevention and control measures as well as the provision of supportive care for complications.

Corticosteroids are often avoided due to their ability to prolong viral replication, as evidenced by observations in patients with Middle East Respiratory Syndrome Coronavirus (MERS-CoV), unless their usage is warranted for other specific indications. As an illustration, in the case of a chronic obstructive pulmonary disease (COPD) exacerbation or septic shock as outlined in the surviving sepsis recommendations⁽¹¹⁾

1) Mild Cases ⁽²³⁾

Supportive treatments (Anti-histamine and Analgesics)

2) Moderate Cases

- Oseltamivir (150 mg BD for 5 days)
- Hydroxychloroquine, Chloroquine (500 mg BD for 14 days) or Ribavirin (for 5 days)

3) Severe Cases

- Oseltamivir (150 mg BD for 5 days)
- Kaletra (Lopinavir/Ritonavir) (for 5 days)
- Hydroxychloroquine, Chloroquine (500 mg BD for 14 days) or Ribavirin (for 5 days)

4) Critical Cases

- Oseltamivir (150 mg BD for 5 days)
- Kaletra (Lopinavir/Ritonavir) (for 5 days)
- Ribavirin (for 5 days)
- Hydroxychloroquine or Chloroquine (for 14 days). ⁽¹³⁾

Plasma therapy:

Plasma therapy involves the utilisation of blood donated by individuals who have successfully recovered from

COVID-19 in order to administer antibodies to people currently undergoing treatment for the same condition.

Currently, the utilization of plasma therapy has been implemented as a treatment modality for individuals diagnosed with COVID-19.

The therapy can also be employed for the purpose of immunizing individuals who are at a heightened risk of infection.

Corticosteroids are often avoided due to their ability to prolong viral replication, as evidenced by observations in patients with Middle East Respiratory Syndrome Coronavirus (MERS-CoV), unless there are specific indications for their usage. As an illustration, in the case of a chronic obstructive pulmonary disease (COPD) exacerbation or septic shock, as outlined in the surviving sepsis recommendations. ⁽²²⁾

Plasma: The primary function of plasma is to facilitate the transportation of nutrients, hormones, and proteins to the specific regions of the body that require them. Additionally, cells expel their metabolic waste products into the plasma. Subsequently, the plasma facilitates the elimination of metabolic waste from the organism.

Plasma cells can be broadly categorised into two main groups based on their lifespan.

a) Short-lived plasma cells, also known as plasma blasts, are cells that undergo proliferation and have a lifespan of approximately 3-5 days.

b) Long-lived plasma cells, on the other hand, are non-proliferating cells that can persist for several months to a lifetime.

Blood plasma is a liquid component of blood that lacks blood cells but retains suspended proteins and other ingredients found in whole blood. It is characterised by its amber colour. Approximately half of the overall blood volume is comprised of blood plasma.

Plasma refers to the fluid component of blood that consists of proteins and salts, within which red and white blood cells, as well as platelets, are suspended.

The plasma component constitutes 55% of the overall blood volume and is mostly constituted of water, salts, lipids, and hormones, with water accounting for approximately 90% of its composition. The substance exhibits a high concentration of many proteins, notably albumin, immunoglobulin, clotting factor, and fibrinogen.

Plasma is composed of around 8-9% solids and 91-92% water. The primary constituents of this substance mostly consist of coagulants, specifically fibrinogen, which play a crucial role in the process of blood clotting. Plasma proteins, including albumin and globulin, play a crucial role in regulating the colloidal osmotic pressure, which is typically maintained at approximately 25mmHg.

Plasma transfusion is an effective therapeutic approach in the treatment of various diseases, including cancer,



particularly in paediatric and adult patients afflicted with leukaemia. The individuals in question are individuals who are currently having liver transplants, bone marrow transplants, and are experiencing serious congenital conditions. The coagulation factors relevant to individuals with haemophilia. The clotting factors utilised for individuals with haemophilia are derived from donated plasma.

Generally, plasma donors must be age above 18 years and weight at least 110 pounds (50kgs). All individuals must pass two separate medical examination, a medical history screening and testing for transmissible viruses, before their donated plasma therapies.

Procedure: The blood obtained from individuals who have successfully recuperated from the coronavirus disease 2019 (COVID-19) has antibodies specific to the causative virus. The given blood undergoes a processing procedure wherein blood cells are separated from plasma, resulting in the isolation of liquid (plasma) and antibodies. These interventions can be administered to individuals diagnosed with COVID-19 in order to enhance their immune response against the virus.

1. Prior to the commencement of plasma therapy, the healthcare team undertakes the necessary preparations to ensure the patient's readiness for the procedure. A member of the health care team proceeds to place a sterile, disposable needle that is attached to a tube (known as an intravenous or IV line) into a vein located in one of the patient's arms.
2. Through the course of the procedure, upon the arrival of the plasma, the aseptic plasma bag is affixed to the tube, facilitating the gradual flow of plasma from the bag into the tube. The completion of the process typically requires a time frame of approximately one to two hours.
3. Following the administration of convalescent plasma, the individual will undergo thorough monitoring. The physician will document the patient's reaction to the therapeutic intervention. The individual may additionally document the duration of hospitalisation required and the necessity for supplementary therapeutic intervention.

Side effects of Plasma therapy

- The most prevalent types of immune-triggered reactions are allergic and anaphylactic reactions, as well as transfusion-related acute lung injury (TRALI) and hemolysis. The degree of side effects might vary, ranging from minor to severe.
- Overload of fluid and citrate toxicity are potential complications that may arise following quick or extensive transfusion.
- The implementation of two distinct viral inactivation procedures results in a significantly reduced probability of viral transmission.
- Various products are known to have unique adverse effects. For instance, the administration of intravenous

immunoglobulin has been linked to the occurrence of aseptic meningitis. Similarly, the use of coagulation factor has been connected with the emergence of inhibitors and thrombotic events.

- The potential for spreading of variant Creutzfeldt Jakob disease through products made from plasma and pooled plasma components remains uncertain at present.
- The presence of a relatively small amount of prion infectivity in the bloodstream of a person with the
- infection will be significantly diminished due to the dilution effect caused by the large volume of plasma units present in the pool.
- One of the drawbacks of plasma therapy is the potential for non-infectious risks associated with transfusion. These risks include transfusion reactions, such as transfusion-related breathlessness and life-threatening allergic reactions accompanied by bronchospasm. These reactions might potentially worsen respiratory symptoms in patients with COVID-19.
- Infections such as Human Immunodeficiency Virus (HIV) and Hepatitis B and C.
- If convalescent plasma therapy will be an effective treatment for covid-19 is not known. You might not experience and benefit. However, plasma therapy might help you recover from the disease.
- Data from several clinical trials, studies and a national access program suggest that convalescent plasma therapy with high antibody levels may lessen the severity or shorten the duration of covid-19 in some people when given early in the disease or in those with weakened immune system. However, more research is needed to decide if convalescent plasma therapy will be an effective treatment for covid-19.

Prevention:

- It is imperative to adhere to a minimum distance of 1 metre from others in order to ensure safety.
- It is strongly advised to consistently use a mask in public settings, particularly when physical separation is not feasible, especially in indoor environments.
- If situated indoors, it is advisable to open a window.
- Frequently practise hand hygiene by either employing soap and water or utilising an alcohol-based hand sanitizer.
- It is recommended that individuals cover their noses and mouths with either their bent elbow or a piece of tissue when coughing or sneezing.
- Individuals experiencing symptoms such as coughing, cold symptoms, and respiratory distress are advised to promptly seek medical assistance.
- This precaution serves to safeguard individuals and mitigate the transmission of viruses and other infectious agents to others. ⁽¹⁴⁾



Fig 1.5: preventive measures of covid-19 ⁽⁴²⁾

Advice:

- The majority of those afflicted with the coronavirus disease will experience spontaneous recovery, and there are also other measures that can be undertaken to safeguard oneself or alleviate symptoms.
- **Care for children:** When youngsters are afflicted with the coronavirus, it is not advisable to administer aspirin to them.
- **Environmental measures:** One potential environmental intervention for alleviating symptoms of throat irritation and cough is the utilisation of a room's humidifier or the exposure to steam generated by a hot shower.
- **Care from Animals:** It is advised to avoid physical contact with animals that are known to be potential carriers of the coronavirus, such as camels, bats, and other wild animals. It might be beneficial to maintain a distance from youngsters.
- **Using Napkins or Hand kerchiefs:** One recommended practice is using handkerchiefs when sneezing, ensuring the mouth is well covered. Additionally, it is advisable to regularly disinfect one's hands by coming into contact with various objects and surfaces^(34,35)

Vaccine:

A vaccine refers to a specific formulation designed to induce immunity against a particular illness by triggering the development of antibodies. Vaccination refers to the process of receiving a vaccine in order to induce immunity against a certain sickness or condition. Vaccinations play a crucial role in maintaining the health and safety of communities by

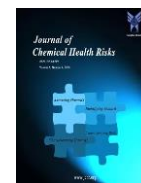
- Supporting herd immunity
- Spreading of disease can be prevented.

All COVID-19 vaccines protect people by making their body recognize a piece of the outside of the Covid-19 virus called "Spike Protein".

Currently approved Covid-19 vaccines are safe and effective.

Most side effects occur of someone getting the vaccine within 6 weeks. FDA needs 8 weeks of safety monitoring.

- 1) Corbevax Vaccine
Manufacturer: Biological E. limited
Vaccine type: Protein subunit
Administration method: Intramuscular injection.
- 2) Covaxin Vaccine
Manufacturer: Bharat Biotech
Vaccine type: Inactivated
Administration method: Intramuscular injection
Research name: BBV152
- 3) Covishield
Manufacturer: AstraZeneca, Serum institute of India
Vaccine type: non-replicating viral vector
Administration method: Intramuscular injection
Research name: AZD1222 (chAdOx1)
Also known as: Oxford, AstraZeneca vaccine.
- 4) Johnson and Johnson Vaccine
Manufacturer: Janssen pharmaceutical companies
Vaccine type: Non replicating viral vector
Administration method: Intramuscular injection
Research name: JNJ-78436735 (Ad26.CoV2. S)
- 5) Moderna Vaccine
Manufacturer: Moderna, NIAID
Vaccine type: RNA
Administration method: Intramuscular injection
Research name: mRNA-1273
- 6) Novavax Vaccine
Manufacturer: Novavax
Vaccine type: Protein subunit
Administration method: Intramuscular injection
Research name: NVX-CoV2373
- 7) Sputnik Light Vaccine
Manufacturer: Gamaleya Research institute
Vaccine type: Non replicating Viral Vector
Administration method: Intramuscular injection
Research name: Sputnik Light
- 8) Sputnik V Vaccine
Manufacturer: Gamaleya Research institute



Vaccine type: Non replicating viral vector
Administration method: Intramuscular injection
Research name: Gam-COVID-Vac
9) Zydus Cadila Vaccine
Manufacturer: Cadila Healthcare Ltd.
Vaccine type: DNA based Vaccine
Administration method: Intradermal Injection
Research name: Zydus Cadila.

Side effects of Vaccination

Side effects to Covid-19 Vaccines reported by people have been mostly mild to moderate and short-lasting.

- Fever
- Fatigue
- Headache
- Muscle pain
- Chills
- Diarrhoea
- Pain at injection site

The chances of any these side effects following vaccination to people differ according to specific Covid-19 Vaccine.

More long-lasting or serious side effects to vaccines are possible but extremely rare. Vaccines are continually monitored for detecting the rare adverse events.⁽¹⁵⁾

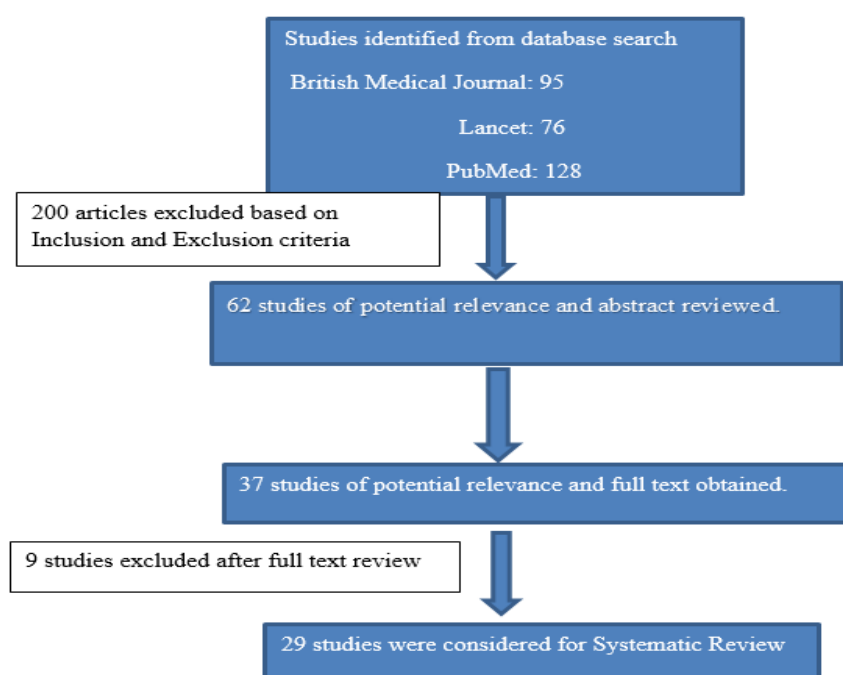
Aims: This study was aimed to address the clinically relevant issues and over view the treatment patterns commonly observed in individuals in the first and second waves who have been diagnosed with covid-19.

Objectives:

- To assess the sign and symptoms of covid-19 in articles.
- To identify the co-morbidities that occurred in both waves.
- To study the different treatment patterns observed in the first and second waves.

Strategy and selection for search criteria

In conducting this Systematic Review, a comprehensive search of the literature was performed, encompassing the period from December 3rd, 2021, with the aim of identifying relevant published publications. A comprehensive literature search was conducted on the PubMed, Lancet, and BMJ databases as part of a systematic review. The subsequent search phrases were employed. "Coronavirus", "Symptoms of Covid-19", "Risk Factors of Covid-19", "First wave of Covid-19", "Second wave of Covid-19", "Treatment of Covid-19", "Prescribing patterns of Covid-19. Following the identification of papers, a total of 200 articles were removed from the study based on predetermined Inclusion and Exclusion criteria. 200 articles were excluded based on Inclusion and Exclusion criteria. After this, 62 studies of potential relevance and abstract were reviewed and 37 studies of potential relevance and full text were obtained. 9 studies were excluded after a full-text review. Hence, a total of 29 papers were chosen for the final analysis based on predetermined criteria for inclusion and exclusion.



3.1 Flow chart Algorithm for database search and article selection

**Study Criteria****Inclusion Criteria**

- Studies performed on human subjects
- Articles published on 2020-2022
- Manuscript titles like-covid-19, prescription patterns, treatment pattern, symptoms, systemic review, complications, first wave and second wave
- Articles of Age group above 18 years
- Articles published in countries like –India, USA, Spain, Nigeria, Italy, UK, California.

Exclusion Criteria

- Articles of age group below 18 years are excluded
- Articles with pregnant women subjects are excluded
- Articles published in countries like – Australia, Africa, Europe.
- Articles of animal studies are excluded.
- We excluded articles of sample size <200.

- Studies on Third wave are excluded.

Analysis of Data:

The final articles were examined in order to get the following information from each: Name of First author, Publication year, Study design, Title, No. of Patients, Symptoms, Comorbidities, Risk factors, Treatment.

Study Design: Systematic Review

Study Duration: November 2021 – May 2022

Study Site: Online databases like PubMed, Lancet, BMJ

Study Sample: 29 articles were collected by key ideas

Key ideas include – Covid-19, Covid-19 symptoms, Covid-19 Comorbidities, First wave of Covid-19, Second wave of Covid-19, Complications of Covid-19, Risk Factors of Covid-19, Treatment of Covid-19, Prescribing patterns of Covid-19.

Authors:

	Authors	Title	Type of Study	Publication Year	Journal
1.	Faxiang Luo et al	Systematic Review and Meta-Analysis of Fear of Covid-19	Systematic Review and Meta-Analysis	11 th June 2021	PubMed
2.	Minah Park et al	A Systematic Review of Covid-19 Epidemiology Based on current	Systematic Review	31 st March 2020	PubMed
3.	Madhav P et al	Prescription pattern among mild to moderate COVID-19 patients in Tertiary care centre; Anil Neerukonda Hospital, Vishakhapatnam	Cross sectional descriptive study	14 th March 2021	PubMed
4.	Simona Iftimie et al	First and Second waves of coronavirus disease-19: A comparative study in hospitalized patients in Reus, Spain	comparative study	March 31 st , 2021	PubMed
5.	Brendan O Kelly et al	Antibiotic prescribing patterns in patients hospitalized with COVID-19: lessons from the first wave	Cohort study	25 th May 2021	PubMed
6.	Matthew E et al	Psychotropic medication prescribing during the COVID-19 pandemic	Quasi-experimental study	11 th October 2021	PubMed
7.	Valentina Orlando et al	Drug utilization profiles and Covid-19	Retrospective study	2021	PubMed
8.	Monica Douglas et al	Impact of COVID-19 on Outpatient Antimicrobial Prescribing Patterns in New York City	Retrospective study	2021	PubMed
9.	Richard Williams et al	Diagnosis of physical and mental health conditions in primary care during the Covid-19 pandemic; a Retrospective cohort study	Retrospective cohort study	23 rd September 2020	PubMed
10.	Kueiyu Joshu Lin et al	Pharmacotherapy for Hospitalized patients with Covid-19; Treatment patterns by Disease Severity	Retrospective study	5 th November 2020	PubMed
11.	Stella Talic et al	Effectiveness of public health measures in reducing the incidence of Covid-19, SARS-CoV-2 transmission and Covid-19 mortality: Systematic Review and Meta-analysis	Systematic Review and Meta-analysis	21 st October 2021	British medical journal
12.	Bart G Pijls et al	Demographic risk factors for Covid-19 infection, Severity, ICU admission and death: a meta-analysis of 59 studies	meta-analysis	14 th December 2020	British Medical Journal



13.	Jonathan H et al	Medication Use Patterns in Hospitalized Patients With COVID-19 in California During the Pandemic	Cohort study	27 th March 2021	British Medical Journal
14.	Daniel Ayoubkhani et al	post-covid syndrome in individuals admitted to hospital with Covid-19: retrospective cohort study	retrospective cohort study	31 st March 2021	British Medical Journal
15.	Albert prats-Urbe et al	Use of repurposed and adjuvant drugs in hospital patients with Covid-19: Multinational network cohort study	cohort study	16 th April 2021	British Medical Journal
16.	Sarah E Daugherty et al	Risk of clinical sequelae after the acute phase of SARS-CoV-2 infection: retrospective cohort study	retrospective cohort study	19 th May 2021	British Medical Journal
17.	Tommy Nyberg et al	Risk of hospital admission for patients with SARS-CoV-2 variant B.1.1.7: cohort analysis	Cohort study	15 th June 2021	British Medical Journal
18.	Hannah R Whittaker et al	GP consultation rates for sequelae after acute Covid-19 in patients managed in the community or hospital in the UK: Population based study	Population based study	23 rd November 2021	British Medical Journal
19.	Ken Cohen et al	Risk of persistent and new clinical sequelae among adults aged 65 years and older during the post-acute phase of SAR-CoV-2 infection: retrospective cohort study	retrospective cohort study	24 th December 2021	British Medical Journal
20.	Yan Xie, Benjamin Bowe et al	Comparative evaluation of clinical manifestations and risk of death in inpatients admitted to hospital with covid-19 and seasonal influenza: cohort study	cohort study	15 th December 2020	British Medical Journal
21.	Benedetta Vai et al	Mental disorders and risk of Covid-19-Related mortality, hospitalization and Intensive Care Unit admission: a systematic review and meta-analysis	systematic review and meta-analysis	15 th July 2021	Lancet
22.	Ting Shi et al	Risk of serious COVID-19 outcomes among adults with asthma in Scotland: a national incident cohort study	cohort study	13 th January 2022	Lancet
23.	Kathleen M Anderson et al	Long-term use of immunosuppressive medicines and in hospital Covid-19 outcomes: a retrospective cohort study using data from the National Cohort Collaborative	retrospective cohort study	15 th November 2021	Lancet
24.	H.G. Gaitan-Duarte et al	Effectiveness of rosuvastatin plus colchicine, emtricitabine/tenofovir and combinations thereof in hospitalized patients with Covid-19; a pragmatic, open-label randomized trial	Randomized control study	20 th December 2021	Lancet
25.	Anna Schultze et al	Risk of Covid-19 related death among patients with Chronic obstructive pulmonary disease or asthma prescribed inhaled corticosteroids; an observational cohort study using the open SAFELY platform	observational study	24 th September, 2020	Lancet
26.	Kunal Nandy et al	Coronavirus disease (COVID-19): A systematic review and meta-analysis to evaluate the impact of various comorbidities on serious events	systematic review and meta-analysis	28 th June 2020	Elsevier
27.	Sarah Steez et al	Temporal trends in primary care recorded self-harm during and beyond the Covid-19 pandemic: Time series analysis of electronic healthcare records for 2.8 million patients in the Greater Manchester Care Record	Retrospective study	1 st November 2021	Elsevier



28.	Hetal Dhruve et al	Prescribing patterns and Treatment Adherence in Patients with Asthma During the COVID-19 Pandemic	Retrospective study	2021	Elsevier
29.	B Riley et al	A short report: Acute, non-COVID related medical admissions during the first wave of COVID-19: A retrospective comparison of changing patterns of disease	Retrospective study	18 th September 2020	Acute Medicine Journal

Table 4.1 Different article collected for systematic review

These are the different articles collected and reviewed of our study.

Symptoms:

S.NO	Authors	Number of patients	Study duration	Symptoms
1.	Simona Iftimie et al	First wave -204 patients Second wave-264 patients	First wave between 15 th to 30 th June Second wave between 1 st to 15 th October	First wave -fever, dyspnea, pneumonia, and cough second wave -renal and gastrointestinal symptoms
2.	Brendan O Kelly et al	292 patients	9 th march to 28 th may 2020	Cough, fever, shortness of breath, fatigue, myalgia, headache, sore throat, diarrhoea, nausea/vomiting, chest pain, decreased level of consciousness, abdominal pain, loss of taste, rhinorrhoea, seizure.
3.	Hannah R Whittaker et al	3851 patients	1 August 2020 and 14 February 2021	loss of smell or taste, or both, fatigue, palpitations, breathlessness, tinnitus, paresthesia, chest pain, muscle pain, lung fibrosis, venous thromboembolism, and renal failure

Table 4.2: covid-19 sign and symptoms of different articles

In Simona Iftimie et al In all waves, the most commonly observed signs and symptoms included fever, dyspnea, pneumonia, and cough. Patients in the second wave had notable distinctions compared to those in the first wave. Specifically, they displayed a heightened incidence of symptoms such as vomiting, asthenia, stomach discomfort, rhinorrhea, and acute kidney failure. Conversely, symptoms such as cough or chills were less frequently observed in this group.

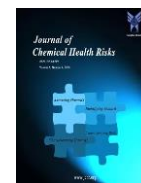
In Brendan O Kelly et al, Among the total of 292 patients, the most commonly reported symptoms include cough, which was observed in 201 individuals (68%); fever, which was experienced by 179 patients (61.3%); shortness of breath, reported by 133 individuals (45.5%); fatigue, noted in 94 patients (32.2%); myalgia, observed in 67 individuals (22.9%); headache, reported by 47 patients (16.1%); sore throat, experienced by 38 individuals (13%); diarrhoea, noted in 34 patients (11.6%); nausea/vomiting, reported by 34 individuals (11.6%); chest pain, observed in 34 patients (11.6%); decreased level of consciousness, noted in 22

patients (7.5%); abdominal pain, experienced by 13 individuals (4.5%); loss of taste, reported by 9 patients (3.1%); rhinorrhoea, observed in 8 patients (2.7%); and seizure, which was reported by only 1 patient (0.3%).

In Hannah R Whittaker et al, The post-COVID-19 consultation rates among patients in the community for general practitioners (GPs) encompassed several symptoms, notably stomach discomfort. Additionally, albeit to a lesser degree, other symptoms such as diarrhea, muscle pain, general pain, tinnitus, nausea, and chest tightness were also observed. On the other hand, there was a noticeable decrease in symptoms such as dyspnea, headache, chest pain, and weariness as time progressed. The prevalence of anxiety and depression, as well as lung fibrosis to a certain degree, exhibited relative stability on a monthly basis. Conversely, the incidence of diabetes, anaemia, venous thromboembolism, and stroke demonstrated a downward trend over the course of time. The frequency of all medication prescriptions shown a decrease throughout the subsequent observation period.

Risk factor:

S.NO	Author	Number of patients	Study duration	Risk factors
1.	Ting Shi et al	4 421 663 adults	March 1, 2020, and July 27, 2021	Asthma, ICU admission, and Death
2.	Ken Cohen et al	133366 patients	January 2019 – 2020	Respiratory failure, Hypertension, Amnesia or memory difficulty, Kidney injury, Mental health, Hypercoagulability, DVT PE PAO, Cardiac



				rhythm disorders, Encephalopathy, Dementia, Type 2 diabetes, CHF, cardiomyopathy myocarditis, Anemia Stroke and sequelae, Coronary disease, Liver test, abnormality Sleep, apnea, Pulmonary hypertension, Atopic dermatitis.
3.	Simona Iftimie et al	204 patients in first wave 264 patients in second wave	First period between 15 th march to 30 th June Second period between 1 st July to 15 th October	Cardiovascular disease, Hypertension, Type 2 diabetes mellitus, Chronic neurological disease, Chronic kidney disease, Chronic lung disease, Cancer, Other infectious diseases, Chronic liver disease, Postpartum, Pregnancy
4.	Sarah E Daugherty et al	Age group 18-65 years patients	January 2019 to 1 April 2020	chronic respiratory failure, cardiac arrhythmia, hypercoagulability, encephalopathy, peripheral neuropathy, amnesia (memory difficulty), diabetes, liver test abnormalities, myocarditis, anxiety, and fatigue
5.	Benjamin Bowe et al	covid-19 between 1 February 2020 and 17 June 2020 (n=3641) and seasonal influenza between 2017 and 2019 (n=12676).	1 February 2020 and 17 June 2020	Acute kidney injury, incident renal replacement therapy, incident insulin use, severe septic shock, vasopressor use, pulmonary embolism, deep venous thrombosis, stroke, acute myocarditis, arrhythmias and sudden cardiac death, elevated troponin, elevated aspartate aminotransferase, elevated alanine aminotransferase, and rhabdomyolysis

Table 4.3: covid-19 risk factors of different articles

In Ting Shi et al, They observed that individuals who have been prescribed two or more courses of oral corticosteroids or have been hospitalized for asthma during the past two years are more likely to have hospitalization due to COVID-19, as well as admission to the intensive care unit or mortality, in comparison to individuals without asthma.

According to the study conducted by Ken Cohen et al, it was projected that among patients aged 65 years and older who were infected with covid-19, around 32 out of every 100 individuals experienced the development of one or more new clinical sequelae throughout the post-acute period, necessitating medical attention. The aforementioned consequences encompass chronic respiratory failure, heart complications (including cardiac arrhythmias and acute coronary syndromes), hypercoagulability, neurological impairments (such as encephalopathy, dementia, cognitive impairments, and stroke), renal dysfunction, diabetes, and anaemia. When comparing persons diagnosed with COVID-19 to those affected by viral lower respiratory tract sickness, it was seen that the disparities in post-acute sequelae were minimal. Notably, there was a statistically significant association between COVID-19 and a higher likelihood of experiencing respiratory failure, post-viral weariness, and dementia. While the risk of persistent and new sequelae for various clinical conditions significantly increased among individuals admitted to the hospital for covid-19, it is important to note that older patients aged 65 years and above who did not require hospital admission for covid-19 were still susceptible to

experiencing persistent or new clinical sequelae during the post-acute phase.

In Simona Iftimie et al, Lastly, In relation to mortality-associated risk factors, distinctions were observed between the initial and subsequent phases. An examination using multiple regression analysis revealed that during the initial wave, mortality was independently associated with advanced age, dyspnea, acute respiratory distress syndrome, diabetes, and cancer. Conversely, during the subsequent wave, mortality was linked to gender, age, acute respiratory distress syndrome, and chronic neurological diseases. This could potentially be indicative of improved patient management for cancer or diabetes mellitus. However, the correlation between mortality and neurological maladies may be attributable to the higher mean age of those who perished during the second wave.

Sarah E Daugherty et al, concluded that Chronic respiratory failure, cardiac arrhythmia, hypercoagulability, encephalopathy, peripheral neuropathy, amnesia (memory difficulty), diabetes, abnormalities in liver tests, myocarditis, anxiety, and exhaustion are among the clinical sequelae that may occur following covid-19.

In Benjamin Bowe et al, Their findings indicate that there was a greater association between covid-19 and several adverse events, including severe septic shock, vasopressor use, pulmonary embolism, deep venous thrombosis, stroke, acute myocarditis, arrhythmias and sudden cardiac death, elevated troponin, elevated aspartate aminotransferase, elevated alanine



aminotransferase, and rhabdomyolysis, in comparison to seasonal influenza. Additionally, Covid-19 was associated with an elevated mortality risk, the requirement for mechanical ventilation, intensive care unit admission, and extended hospitalisation. Black

patients with obesity, diabetes mellitus, and chronic kidney disease, as well as adults aged 75 and older with chronic kidney disease and dementia, had mortality rates for covid-19 that were higher than those observed for seasonal influenza.

Co-morbidities

S.NO	Authors	Number of patients	Study duration	Co-morbidities
1.	Albert prats-Urbe et al	303264 patients	January 2020 to December 2020	Anemia, Anxiety disorder, asthma, atrial fibrillation, chronic liver disease, COPD, Dementia, Diabetes Mellitus, GERD, Heart disease, Heart failure, Hyperlipidaemia, Hypertensive disorder, Insomnia, Ischemic Heart Disease, Low back pain, Malignant neoplastic disease, Osteoarthritis of hip, Osteoarthritis of knee, Peripheral vascular disease, Renal impairment, Venous thrombosis, Viral hepatitis.
2.	Ken Cohen et al	13366 patients	January 2019 – 2020	Pervious co-morbidities: AIDS, Alcohol abuse, Cerebrovascular Disease, Chronic pulmonary disease, Coagulopathy, Congestive Heart failure, Dementia, Depression, Drug abuse, Hypertension, Hypothyroidism, Liver disease, Peptic ulcer disease, paralysis.
3.	Sarah E Daugherty et al	Age group 18-65 years patients	January 2019 to 1 April 2020	Alzheimer dementia, asthma, cystic fibrosis, immunodeficiency, pulmonary fibrosis, sickle cell disease, smoking, Type 1 diabetes, Type 2 diabetes
4.	Brendan O Kelly et al	292 patients	9 th march to 28 th may 2020	chronic illness, cardiac disease, hypertension, respiratory illness, dyslipidaemia, cognitive impairment, diabetes mellitus, ischaemic heart disease, psychiatric diagnosis, chronic kidney disease, asthma, COPD, osteoarthritis, malignancy, haematological, congestive cardiac failure, stroke, obesity, solid organ transplant, liver cirrhosis, HIV, bone marrow transplant, Radiology, normal appearance, consistent with viral pneumonitis
5.	Anna Schultze et al	148 557 people with COPD and 818 490 people with asthma	March to May 2020	Chronic kidney disease, hypertension and other disease, diabetes, cancer
6.	Daniel Ayoubkhani et al	47780 patients	31 th august to 30 September 2020	Respiratory, cardiovascular, metabolic, kidney, and liver diseases
7.	Kathleen M Anderson et al	231830 patients	January 1 st 2020 to June 11 th 2021	Diabetes, pulmonary disease, and renal disease

Table 4.4: covid-19 co-morbidities of different articles

In Albert prats-Urbe et al, the common comorbidities such as Anemia, Anxiety disorder, asthma, atrial fibrillation, chronic liver disease, COPD, Dementia, Diabetes Mellitus, GERD, Heart disease, Heart failure, Hyperlipidaemia, Hypertensive disorder, Insomnia, Ischemic Heart Disease, Low back pain, Malignant neoplastic disease, Osteoarthritis of hip, Osteoarthritis of knee, Peripheral vascular disease, Renal impairment, Venous thrombosis, Viral hepatitis are identified in this article.

In Ken Cohen et al, unmatched 2020 and 2019 comparison groups, Individuals with SARS-CoV-2 infection were more likely to be older, male, have a

lower socioeconomic status index, be of black or Hispanic race, reside in midwestern and northeastern US states, have a pre-existing comorbidity, have had a longer inpatient hospital stay the previous year, and have visited a primary care physician, cardiologist, or nephrologist more frequently.

In Sarah E Daugherty et al, the common co-morbidities such as Alzheimer dementia, asthma, cystic fibrosis, immunodeficiency, pulmonary fibrosis, sickle cell disease, smoking, Type 1 diabetes, Type 2 diabetes are identified in this article.

In Brendan O Kelly et al, Comorbidities aligned with poor outcomes in COVID-19 like diabetes mellitus and



obesity were seen in patients, respectively. Other comorbidities are included chronic illness, cardiac disease, hypertension, respiratory illness, dyslipidaemia, cognitive impairment, diabetes mellitus, ischaemic heart disease, psychiatric diagnosis, chronic kidney disease, asthma, COPD, osteoarthritis, malignancy, haematological, congestive cardiac failure, stroke, obesity, solid organ transplant, liver cirrhosis, HIV, bone marrow transplant, Radiology, normal appearance, consistent with viral pneumonitis.

In Anna Schultze et al, The prevalence of the majority of comorbidities was lowest among individuals prescribed only SABA and highest among those prescribed high-dose ICS; other co-morbidities include

chronic kidney disease, hypertension, diabetes, and malignancy.

In Daniel Ayoubkhani et al, Individuals diagnosed with COVID-19 exhibited a greater propensity for comorbidity than the general population. This was evidenced by a higher prevalence of all assessed pre-existing conditions, including hypertension, significant adverse cardiovascular events, respiratory disease, and diabetes, as well as prior hospital admissions.

In Kathleen M Anderson et al, Comorbidities such as diabetes (23%), pulmonary disease (17%), and renal disease (13%), were the most prevalent. The prevalence of comorbidities was higher among patients with immunosuppression.

Treatment:

S.NO	Authors	Number of patients	Study duration	Treatment
1.	Madhav P et al	188 patients	April 2020 to August 2020.	Ivermectin, Doxycycline, Paracetamol, Azithromycin, Multivitamin, Vitamin C, Pantoprazole, Dexamethasone, Favipiravir, Hydroxychloroquine, Amoxicillin, Enoxaparin
2.	Jonathan H et al	22 896 patients	March 10, 2020, to December 31, 2020	ACEIs/ARBs, Azithromycin, Colchicine, Hydroxychloroquine, Enoxaparin, Heparin, Hydrocortisone, Tocilizumab, Dexamethasone, Remdesivir.
3.	Simona Iftimie et al	204 patients in 1 st wave 264 patients in 2 nd wave	First period in between 15 th march to 30 th June Second period in between 1 st July to 15 th October	Non-invasive mechanical ventilation, Invasive mechanical, ventilation, High-flow oxygen therapy, Conventional oxygen therapy, Anticoagulants, Corticosteroids
4.	Albert prats-Urbe et al	303264 patients	January 2020 to December 2020	Hydrochloroquine, Dexamethasone Azithromycin Tocilizumab Ritonavir Remdesivir
5.	Matthew E. Hirschtritt et al	2,405,824 KPNC members	December 1, 2017 and June 30, 2020	Antidepressants, benzodiazepines, hypnotics, statins, mood stabilizers, stimulants, and trazodone.
6.	Kathleen M Anderson et al	231830 patients	January 1 st 2020 to June 11 th 2021	Any rheumatological drug, Glucocorticoid with rheumatological condition, Interleukin inhibitor, JAK inhibitor, Rituximab with rheumatological condition, TNF inhibitor, Other selective immunosuppressants Any antimetabolite drug Azathioprine, Calcineurin inhibitor, Glucocorticoid with organ transplant, Mycophenolic acid, Any cancer drug, Cyclophosphamide, Anthracycline, Checkpoint inhibitor, Protein kinase inhibitor, Other antineoplastics Targeted cancer therapy, Rituximab with cancer
7.	Hannah R Whittaker et al	456002 patients	1 August 2020 and 14 February 2021	Bronchodilators, Diuretics Inhaled, corticosteroids, Neuropathic pain drugs, NSAIDs, Opiates (any) Opiates (strong) Opiates (weak) Paracetamol
8.	H.G. Gaitan-Duarte et al	994 patients	August 2020 and March 2021	emtricitabine with tenofovir disoproxil fumarate (FTC/TDF, 200/300 mg given orally for 10 days), colchicine plus rosuvastatin (COLCH+ROSU, 0.5 mg and 40 mg given orally for 14 days)
9.	Valentina Orlando et al	1532 individuals in compania who tested positive for	26 February 2020 to 30 March 2020	Aluminium, calcium and magnesium, Proton pump inhibitors, peptic ulcers, Antibiotics, Biguanide, Vitamin D and analogues, Heparin



		covid-19 on 30 march 2020 were identified		group, Platelet-aggregation inhibitors, Folic acid and derivatives, Sulfonamides, blocking agents, selective, Dihydropyridine derivatives, ACE inhibitors and diuretic, Angiotensin-II receptor blockers, Angiotensin-II receptor blockers and diuretics, HMG CoA reductase inhibitors, Glucocorticoids, Thyroid hormones, Penicillins with extended spectrum, Combinations of penicillins, Third-generation cephalosporins, Macrolides, Fluoroquinolones, Other antibacterial, Antimycotic for systemic use, Acetic acid derivatives, Propionic acid derivatives, Other anti-inflammatory and antirheumatic agents, non-steroidal anti-inflammatory drugs, Preparations inhibiting uric acid, Other antiepileptics, Selective serotonin reuptake inhibitors, Other antidepressants, Adrenergics in combination with corticosteroids, Glucocorticoids, Anticholinergics, Piperazine derivatives, Other antihistamines for systemic use
10.	Kueiyu Joshu Lin et al	2821 patients hospitalized for covid-19	1 march to 24 may 2020	Hydroxychloroquine, azithromycin, darunavir/cobicistat, interferon-beta, and tocilizumab, angiotensin-converting enzyme inhibitors (ACEIs), angiotensin receptor blockers, statins, antibiotics or anti-viral agents for other specific viruses, anticoagulants, proton pump inhibitors (PPIs), and H2-receptor antagonists (H2RAs)
11.	Monica Douglas et al	2019-288 patients 2020-305	March to May 2019-2020	Penicillin, Ampicillin, Amoxicillin, Cephalosporins Cephalexin, Cefuroxime, Cefdinir, Cefixime, Cefpodoxime, Fluoroquinolones Ciprofloxacin, Levofloxacin, Macrolides Azithromycin, Clarithromycin, Other antibiotics, Clindamycin, Doxycycline, Metronidazole, Nitrofurantoin, Vancomycin, Antiviral agents Acyclovir, Famciclovir, Valacyclovir, Oseltamivir, Hydroxychloroquine

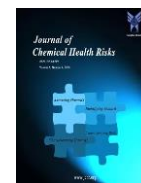
Table 4.5: covid-19 treatment of different articles

The study conducted by Madhav P et al. identified the following as the most frequently prescribed medications: vitamin C (98.9%), multivitamin (98.4%), ivermectin (95.7%), doxycycline (94.7%), paracetamol (80.9%), azithromycin (85.1%), pantoprazole (66.5%), enoxaparin (16%), amoxycillin (13.3%), favipiravir (13.3%), and hydroxychloroquine (9%). Ivermectin is the most frequently prescribed antibiotic at 95.7%, followed by doxycycline at 94.7%, azithromycin at 85.1%, and amoxycillin at 13.3%. "Zincovit" was the most frequently prescribed multivitamin brand (37.84 percent), followed by "Becozinc" (28.65 percent), "Fours B" (6.49%), "Supradyn" (5.41%), and "A to Z" (2.70%).

In a study conducted by Jonathan H et al during the COVID-19 pandemic, it was shown that antimicrobials, specifically azithromycin and hydroxychloroquine, were administered to over 40% of patients who were admitted to the hospital. By June, use was below 30% and 5%, respectively. The utilisation of enoxaparin consistently above 50% throughout the year 2020 due to

its dual functionality in both thrombosis prophylaxis and the treatment of thrombophilia induced by COVID-19. The utilisation of dexamethasone and remdesivir has experienced significant growth. One plausible hypothesis is that the utilisation of remdesivir may have been influenced by its availability, particularly during the initial stages of the pandemic when it was mostly accessible through clinical studies conducted within the UC system. The utilisation of hydroxychloroquine experienced a significant decline, dropping from an initial rate of 40% to a subsequent level below 5% during a span of two months. A preliminary study undertaken during the early stages of the pandemic exhibited a propensity towards the use of hydroxychloroquine; however, subsequent larger-scale controlled investigations conducted thereafter failed to provide any discernible advantages.

According to Simona Iftimie et al, patients in the second wave have a higher frequency of receiving non-invasive mechanical ventilation and corticoids, whereas the use



of invasive mechanical ventilation, traditional oxygen therapy, and anticoagulants is comparatively lower..

In Albert prats-Urbe et al, Common repurposed drugs were hydroxychloroquine (used in from <5 (<2%) patients s in China to 2165 (85.1%) in Spain), azithromycin (from 15 (4.9%) in China to 1473 (57.9%) in Spain), combined lopinavir and ritonavir (from 156) (<2In the study conducted by Albert Prats-Urbe et al., it was observed that the utilisation of certain repurposed drugs varied across different countries. For instance, the usage of hydroxychloroquine ranged from less than 2% of patients in China to 85.1% in Spain. Similarly, the administration of azithromycin increased from 4.9% in China to 57.9% in Spain. The combined use of lopinavir and ritonavir also exhibited variations, with less than 2% in the VA-OMOP US, 34.9% in South Korea, and 50.5% in Spain. Conversely, umifenovir was not utilised in the US, South Korea, and Spain, but was administered to 78.3% of patients in China. The utilisation of supplementary medications shown significant variation, with the top five treatments employed being enoxaparin, fluoroquinolones, ceftriaxone, vitamin D, and corticosteroids. The utilisation of hydroxychloroquine experienced a notable surge during the period from March to April 2020, followed by a substantial fall from May to June, with subsequent maintenance at a low level for the remainder of the year. The utilisation of dexamethasone and corticosteroids exhibited a consistent upward trend throughout the year 2020.in the VA-OMOP US to 2,652 (34.9%) in South Korea and 1285 (50.5%) in Spain), and umifenovir (0% in the US, South Korea, and Spain and 238 (78.3%) in China). Use of adjunctive drugs varied greatly, with the five most used treatments being enoxaparin, fluoroquinolones, ceftriaxone, vitamin D, and corticosteroids. Hydroxychloroquine use increased rapidly from March to April 2020 but declined steeply in May to June and remained low for the rest of the year. The use of dexamethasone and corticosteroids increased steadily during 2020.

According to the study conducted by Hirschtritt et al. (2020), during the initial 13-week period of the COVID-19 outbreak (March 4, 2020 to June 2, 2020), a notable proportion of patients, specifically 8.9%, obtained at least one prescription for depressive medication. Additionally, 0.5% of patients completed prescriptions for hypnotics, 2.5% for benzodiazepines, and 2.0% for trazodone. Antidepressants (+1.5%) and trazodone (+5.8%), according to Matthew E. Hirschtritt et al.

After adjusting for prior-year trends, there was a notable rise in the rates of antidepressant prescriptions (+1.5%) and trazodone prescriptions (+5.8%) when comparing the most recent 13-week period (December 3, 2019 to March 3, 2020) with the preceding year. During the identical time frame, there was a reduction in the use of benzodiazepines by 3.6% and hypnotics by 3.5%. The

utilisation of antidepressants, trazodone, mood stabilisers, antipsychotics, stimulants, and statins shown an upward trend during the period from mid-February to late March 2020, when compared to the preceding year.

In Kathleen M Anderson et al Out of the adults who were admitted to the hospital, a total of 16,494 individuals (7%) possessed active medication records for immunosuppressive medications. These prescriptions encompassed a variety of types, including those generally prescribed for rheumatological conditions (5366 patients, accounting for 33% of the total), antimetabolite pharmaceuticals (4288 patients, accounting for 26%), and medications specifically used for cancer therapy (3569 patients, accounting for 22%). According to the study conducted by Whittaker et al., the pharmaceuticals most frequently recommended for individuals diagnosed with covid-19 for a duration of four weeks or more were opiates (2.2% of patients), paracetamol (1.8%), and non-steroidal anti-inflammatory medicines (1.6%). The researchers observed the most significant variation in paracetamol prescription rates following the onset of the COVID-19 pandemic compared to the corresponding period twelve months prior. Patients who were hospitalised with Covid-19 were additionally administered bronchodilators, neuropathic pain medications, and mild opioids.

The study conducted by H.G. Gaitan-Duarte et al. examines the efficacy of combining FTC/TDF+COLCH+ROSU in reducing the risk of 28-day death and the requirement for invasive mechanical ventilation in patients with pulmonary impairment due to COVID-19 who are admitted to the hospital. Additional randomised controlled trials are necessary to conduct a comparative analysis of the efficacy and cost of treatment with this combination in contrast to other pharmaceuticals that have demonstrated a reduction in mortality rates associated with SARS-CoV-2 infection. Furthermore, it is imperative to assess the utility of this combination in patients who are on chronic statin therapy.

In the study conducted by Valentina Orlando et al, it was observed that initial findings indicated a possible pro-infective impact of certain medications. There are two categories of pharmaceuticals that have been associated with this phenomenon, namely angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin II receptor blockers (ARBs). The observed consequences could potentially arise from the interaction between severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causative agent of COVID-19, and ACE-2 receptors located in the pulmonary system. However, it is important to note that this hypothesis is currently a subject of debate. In the C19G dataset, it was observed that a total of twenty-three pharmacological ATC II



groups and thirty-nine ATC IV groups had a prevalence exceeding 3%. The C19G and GPG had the highest unadjusted and adjusted prevalence rates of drug use among the ATC II groups, specifically for drug categories J01, A02, C09, M01, B01, and R03.

According to the study conducted by Kueiyu Joshu Lin et al, individuals classified as severity level 5 had a 3.53-fold higher likelihood of being prescribed a prescription intended for the treatment of COVID-19, in comparison to patients categorised as severity level 1. Additional factors that were found to be indicative of treatment outcomes included the presence of fever, low levels of oxygen saturation, the existence of co-morbidities, and elevated levels of inflammatory biomarkers. The

utilisation of commonly prescribed drugs for COVID-19 has witnessed a significant decline, whilst the administration of remdesivir and therapeutic anticoagulants has exhibited an upward trend throughout the duration of the study.

According to Monica Douglas et al., the medications that exhibited higher prescription rates during the early surge of the COVID-19 pandemic were cefpodoxime, hydroxychloroquine, doxycycline, and sulfamethoxazole-trimethoprim. In 2020, antimicrobial medicines such as azithromycin, hydroxychloroquine, doxycycline, cefpodoxime, and oseltamivir were administered for the treatment of COVID-19, which presented with antimicrobial indications.

Adherence:

S.NO	Authors	Number of patients	Study duration	Adherence			
1.	Hetal Dhruve et al	1132 patients	January 2019 to January 2020		2019	2020	
				Non-adherence	20.5%	22.0%	
				Poor-adherence	28.0%	19.8%	
				Sub optimal adherence	17.5%	16.2%	
				Good adherence	33.9%	42.0%	

Table 4.6: Adherence of Covid-19 Treatment in article

According to the study conducted by Hetal Dhruve et al, the rates of adherence to inhaled corticosteroids (ICS) continue to be low. Nevertheless, a slight improvement in adherence was noted during the initial year of the COVID-19 pandemic. The rates of salbutamol prescriptions had a decline during the aforementioned time frame, while there has been a consistent increase in the number of prescriptions for peak flow metres. In March 2020, there was a significant surge in national prescriptions of inhaled corticosteroids (ICS), demonstrating a notable increase of 49.9% when compared to the preceding month of February 2020. The study population consisted of 1132 patients, of whom 762 received ICS treatment during the course of both years. In 2020, there was a notable improvement in

adherence to inhaled corticosteroids (ICS), as seen by an increase in the percentage of patients achieving "good adherence" (defined as adherence of 75% or more) from 33.9% to 42.0%. The increase observed in March 2020 mostly resulted from enhanced compliance rather than the influence of several inhalers. The most substantial enhancements in adherence were observed in individuals of the female gender and those of advancing age. In March 2020, there was a comparable increase in the utilisation of salbutamol. Nevertheless, there was a general decline in the number of salbutamol prescriptions for the entirety year 2020. The data presented by national authorities revealed a gradual rise in the utilisation of peak flow metres throughout the year 2020.

Lockdown:

S.NO	Authors	Number of patients	Study duration	Lockdown
1.	Sarah Steez et al	13,148 patients	1 January 2019 to 31 May 2020	1st March to 31st May 2020: first national lockdown 1st June to 30th July 2020: stage 1 of reopening 1st August to 31st October 2020: GM regional restrictions and schools reopening 1st November to 31st December 2020: second national lockdown and regional restrictions 1st January to 29th February 2021: third national lockdown 1st March to 31st May: phased easing of restrictions including schools and colleges reopening

Table 4.7: Lockdowns of Covid-19 in article

According to the study conducted by Sarah Steez et al, the initial nationwide lockdown was implemented from March 1st to May 31st, 2020. Subsequently, the first

stage of reopening occurred from June 1st to July 30th, 2020. During the specified time frame spanning from August 1st to October 31st, 2020, regional restrictions



imposed by GM (presumably referring to the government or a relevant governing body) were implemented, alongside the reopening of schools. Subsequently, from November 1st to December 31st, 2020, a second national lockdown was enforced, accompanied by additional regional restrictions.

Following this, from January 1st to February 29th, 2021, a third national lockdown was instituted. Lastly, from March 1st to May 31st, a gradual relaxation of restrictions occurred, including the reopening of schools and colleges.

Comparison of first wave and second wave:

S.NO	Authors	Number of patients	Study duration	Comparison
1.	Simona Iftimie et al	204 patients in first wave 264 patients in second wave	First period between 15 th march to 30 th June Second period between 1 st July to 15 th October	The patients who died were significantly older than the survivors and those who died in the second wave were older than those in the first wave. The most frequent signs and symptoms in both waves were fever, dyspnea, pneumonia, and cough, and the most relevant comorbidities were cardiovascular diseases, type 2 diabetes mellitus, and chronic neurological diseases. Patients from the second wave more frequently presented renal and gastrointestinal symptoms. Empirical data would suggest that this second wave differs from the first in such factors as age range and severity of the disease.

Table 4.8: Comparison of first and second waves of Covid-19 in article

According to the study conducted by Simona Iftimie et al, it was seen that the individuals who succumbed to the illness were notably advanced in age compared to the survivors. Furthermore, it was found that the patients who passed away during the second wave were of higher age in comparison to those who passed away during the initial wave. The prevailing indicators and manifestations observed during both waves encompassed fever, dyspnea, pneumonia, and cough. Moreover, the most notable coexisting medical conditions were cardiovascular illnesses, type 2 diabetes mellitus, and chronic neurological diseases. Patients in the second wave exhibited a higher incidence of renal and gastrointestinal problems. Based on empirical evidence, it can be inferred that the characteristics of this second wave diverge from those of the initial wave, particularly in terms of age distribution and the gravity of the illness.

Conclusion:

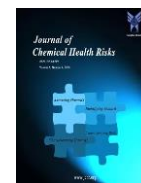
Younger adults are disproportionately affected during the second phase, while older adults with co-morbidities are more significantly impacted during the first. Fever, congestion, shortness of breath, headache, sore throat, and fatigue are the most prevalent symptoms in both waves; however, the incidence of renal and gastrointestinal symptoms is higher in the second wave. While symptomatic treatment is administered during both waves, the second wave necessitates the use of corticosteroids and oxygen therapy primarily due to respiratory complications.

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